I. REMARKS

The final Office Action dated December 31, 2010, has been received and carefully noted. The following remarks are submitted as a full and complete response thereto.

Claims 1-3 and 5-42 are pending. Claims 3, 10-18, and 21-42 are withdrawn.

No amendments to the specification or claims are made at this time.

Claims 1-2, 5-9, 19 and 20 are rejected under 35 U.S.C. §103(a) as being unpatentable over Tsuru (EP 0 376 331, hereinafter "Tsuru") in view of Holmberg (WO 01/66088, hereinafter "Holmberg"). Applicants traverse the rejection.

Claim 1 of the present application is directed to a "solid drug delivery composition comprising one or more NO-donating Non Steroidal Antiinflammatory Compound (s) (NO-donating NSAID(s)) absorbed into porous particles, wherein the porous particles comprise a member selected from the group consisting of: dibasic calcium phosphate, anhydrous, having a Ca to P ratio of 1; microcrystalline cellulose; pregelatinised starch; calcium silicate; magnesium aluminometasilicate; and mixtures thereof." Claims 2, 5-9, 19, and 20 depend from independent claim 1.

Applicants submit that Tsuru does not teach or suggest the presently claimed invention. For example, Applicants submit that Tsuru discloses slow release drug delivery granules comprising porous granules of a calcium phosphate compound having a Ca to P (Ca/P ratio) of 1.3 to 1.8 (page 2, line 49). As noted previously, Applicants submit that the calcium phosphate disclosed in Tsuru refers to salts containing calcium ions (Ca^{2+}), together with an orthophosphate ion (PO_4^{3-}) or pyrophosphates ($P_2O_7^{4-}$), and the atomic ratio Ca/P is always greater than 1. For

example, Applicants submit that hydroxyapatite (disclosed in Example 1 of Tsuru) has the formula $Ca_5(PO_4)_3(OH)$ and an atomic ratio Ca/P of 1.67, and tricalcium phosphate (disclosed in Example 3 of Tsuru) has the formula $(Ca)_3(PO_4)_2$ and an atomic ratio Ca/P of 1.5. Further, Applicants submit that Tsuru also fails to teach or suggest the other porous particles of claim 1, in particular microcrystalline cellulose, pregelatinised starch, calcium silicate, and magnesium aluminometasilicate, or mixtures thereof. In addition, Applicants note that the porous particles of Tsuru do not appear to be commercially available materials, as they have to be prepared by firing at 700°C porous hydroxyapatite granules.

Applicants respectfully disagree with the Examiner's assertion that "[o]ne of ordinary skill in the art at the time the invention was made would have been motivated to make such a composition because it results in controllable and good prolonged effect of the drug release, as explained by Tsuru." Applicants also disagree with the Examiner's statement that one of ordinary skill in the art would have expected a calcium phosphate granule with a Ca/P ratio of greater than 1 (such as 1.3, as disclosed in Tsuru) to have the same properties as a calcium phosphate granule with a Ca/P ratio of 1, as presently claimed.

Applicants submit note Table 1 on page 7 of Tsuru, which shows that porous hydroxyapatite granules impregnated with ADRIACIN (trade name for doxorubicin sulfate) (hydroxyapatite/ADRIACIN, 1:1) maintain a residual amount of ADRIACIN of 49.8% after six hours and 13.6% after 24 hours. Applicants note the present specification discloses dissolution testing of Compound 7, which comprises dibasic calcium phosphate anhydrous (Fujicalcin, which has a Ca/P ratio of 1) porous

particles and compound (Ia) (Fujicalcin/compound (Ia), 1:1.25). After 60 minutes, compound (Ia) is almost completely released, in an amount of 97.8% (or a 2.2% residual amount of compound (Ia)). Applicants summarize the findings of Tsuru and the present application in the following chart:

	TSURU % of residual active agent (ADRIACIN) in the liver	**PRESENT APPLICATION % of residual active agent (compound (Ia) impregnated in the granules**
Time	*Hydroxyapatite granules/ADRIACIN* ***(1:1)***	*Anhydrous dibasic calcium phosphate/compound (Ia)* ***(1:1.25)***
60 minutes (1 hour)		2.2% (or 97.8% released)
6 hours	49.8	
24 hours	13.6	
48 hours	8.2	

Applicants use Composition 7 of the present application as a comparative example to the formulation disclosed in Example 1 of Tsuru, because Composition 7 has a similar ratio of porous granules/active agent (1:1.25 in the present application, compared to 1:1 in Tsuru). Applicants note that all of the compositions described in the present application have a similar quick release properties, unlike the compositions in Tsuru, which have slow release properties.

Applicants further disagree with the Examiner's previous assertion that the comparison of drug release properties of the granules of the present application to the granules of Tsuru is not relevant to show a distinction between the prior art and the present application, since one variable relates to release rates and the other relates to volume released. Applicants respectfully submit that the above reported information refers to the same variables: the amount of impregnated active principle released from the porous materials. Applicants submit that the above Table clearly

shows that the calcium phosphate described in Tsuru (which has a Ca/P ratio above 1 and has slow release properties) has different properties compared to the anhydrous dibasic calcium phosphate of the presently claimed invention, which has a Ca/P ratio of 1 and has fast release properties.

Applicants submit that Holmberg does not fulfill the deficiencies of Tsuru. For example, Applicants submit that Holmberg discloses a pharmaceutical composition in the form of an emulsion pre-concentrate, comprising one or more NO-releasing NSAIDs, one or more surfactants, and optionally an oil or semi-solid fat (page 4, lines 6-12). Holmberg discloses NO-releasing naproxen (formula (Ia), page 8). However, there is no prima facie case of obviousness with the combination of Holmberg with Tsuru, as Holmberg, like Tsuru, fails to teach or suggest the use of porous particles having a Ca/P ratio of 1.

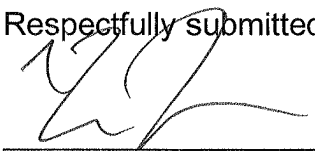
For at least the above reasons, Applicants submit that the presently claimed invention is patentable over Tsuru and Holmberg. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-2, 5-9, 19 and 20 under 35 U.S.C. § 103(a).

II. CONCLUSION

Applicants respectfully submit that this application is in condition for allowance and such action is earnestly solicited. If the Examiner believes that anything further is desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below to schedule a personal or telephone interview to discuss any remaining issues.

In the event this response is not timely filed, the Applicants hereby petition for an appropriate extension of time. The fee for this extension, along with any other additional fees which may be required with respect to this response, may be charged to Deposit Account No. 01-2300, referencing Attorney Docket No. **026220-00054**.

Respectfully submitted,



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